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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/758,936

01/14/2004

Douglas D. Burkett

65879-5008

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7590

11/30/2007

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EXAMINER

WILDER, CYNTHIA B

ART UNIT

PAPER NUMBER

1637

MAIL DATE

DELIVERY MODE

11/30/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/758,936

Applicant(s)

BURKETT, DOUGLAS D.

Examiner

Cynthia B. Wilder, Ph.D.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>6/25/2007</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's species election in the reply filed on 9/18/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1 and 2 have been amended. Claims 1-5 are pending. All of the arguments filed 6/25/2007 have been thoroughly reviewed and considered but are deemed moot in view of the new grounds of rejections necessitated by applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

**This action is made FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Previous Rejections***

3. The prior art rejections under 35 USC 103(a) are withdrawn in view of the new grounds of rejections necessitated by Applicant's amendment of the claims.

#### ***New Ground(s) of Rejections***

**THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S  
AMENDMENT OF THE CLAIMS:**

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

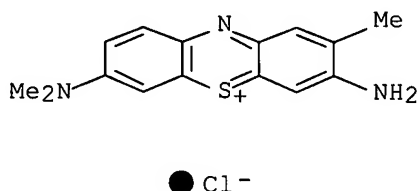
6. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mashberg et al (citation made of record in the prior Office action) in view of Malmros et al (5,372801, December 1994, cited in IDS filed 1/12/2007) and further in view of Rosin (citation made of record in prior Office actions).

Regarding claims 1-2, Mashberg et al teach a prognostic method for early prediction of eventual development of epithelial invasive cancer (oropharyngeal squamous cancers), said method comprising: (a) applying to tissue a staining dye (toluidine blue) that is selectively retained by mitochondria of neoplastic and preneoplastic cells; (b) identifying clonal patches of said tissue by visually examining said

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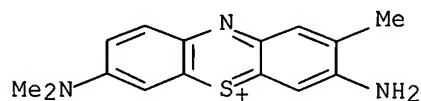
tissue for stained tissue sites (page 345, section entitle "Vital Staining", col. 1, beginning at the second full paragraph to page 347, column 1, lines 1-3); (c) resecting tissue in the locus of said patches for subsequent histopathological analysis (page 347, beginning at col. 1, first full paragraph to page 349, column 1, lines 1-28). Mashberg et al teach that the staining dye is useful because it clinically stains neoplastic and preneoplastic cells (malignant and premalignant cells), but not normal mucosa (page 345, lines 28-29 and serves as a guide to biopsy by localizing tumor cells within the area of erythroplasia (page, 346, 13<sup>th</sup> through 15<sup>th</sup> lines from bottom of column 2).

Mashberg et al teach wherein the staining dye is toluidine Blue (page 345). Mashberg et al do not expressly teach that the toluidine Blue is toluidine blue O having the chemical abstracts service (CAS) registry number 92-31-9 with the chemical structure:



However, given the use of the toluidine blue, one of ordinary skill in the art would assume that the toluidine blue of Mashberg is the same as that of the instant invention. Nonetheless, Malmros et al teach a biological stain composition for in situ delineation of epithelial cancer (col. 2), wherein the stain composition comprises toluidine blue O having the CAS registry number 92-31-9 with the chemical structure (see appendix A):

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The chemical structure being phenothiazin-5-ium, 3-amino-7-(dimethylamino)-2-methyl-, chloride.

Mashberg et al in view of Malmros et al do not expressly teach wherein DNA is extracted from the resected tissue and examined for allelic losses or mutation of tumor suppressor genes.

Rosin et al teach method for the analysis of a biopsy tissue sample to identify genetic changes critical to the progression and non-progression of premalignant lesions into epithelial invasive cancer (oral epithelial dysplasia). Rosin identifies the problem with limiting diagnosis of a cancerous or precancerous condition based on biopsy and pathohistological techniques as taught by Mashberg (see page 1, col. 2, "Introduction") and provides motivation for solving the problem by further performing microsatellite analysis to determine loss of heterozygosity at critical loci (claim 2). Rosin et al teach wherein the method comprises obtaining paraffin-embedded biopsy tissue samples confirmed by histological diagnosis and at least two pathologists as hyperplasia or mild or moderate dysplasia; microdissecting tissue in the locus of areas identified as hyperplasia, dysplasia, or tumor; extracting DNA from the dissected tissue and determining by polymerase chain-based microsatellite analysis whether the dissected tissue exhibits allelic losses (Abstract and page 358, col. 1, beginning at the second full paragraph (section entitle "sample collection) to column 2, sections entitled "Tissue Microdissection and DNA Extraction" and "LOH analysis"). Rosin et al teach that this

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method is a more sensitive technique for studying clonal changes in tumors and premalignant lesions. Rosin et al further teach that the advantage of this procedure is that it requires only small quantities of DNA yet yields valuable data on the loss of chromosomal regions that contain putative suppressor genes. Rosin et al states that hence, information critical to genetic events can be obtained even before the identification of the actual suppressor gene (page 357, column 2, third full paragraph).

Therefore in view of foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have combined the polymerase chain-based microsatellite analysis method of Rosin et al with the staining diagnosis method of Mashberg et al. as a prognostic method for the early prediction of eventual development of invasive cancer. One of ordinary skill in the art would have been motivated to do so for the advantages taught by Rosin et al that the polymerase chain-based microsatellite analysis method is a more sensitive technique for studying clonal changes in tumors and premalignant lesions in that the method requires only small quantities of DNA yet yields valuable data on the loss of chromosomal regions that contain putative suppressor genes (page 357, column 2, third full paragraph).

Regarding claims 3-5, Rosin et al teach wherein the microsatellite analysis is conducted at any one or a combination of chromosomes 3p and 9p and 17p (see abstract and page 358, col. 1, first full paragraph and section entitled "LOH analysis"). Rosin further teaches that LOH of 3p and/or 9p are frequently lost in oral tumors and head and neck tumors and is therefore a prerequisite for progression and may be used

as an initial screening for assessing risk of epithelial premalignancies (see discussion as pages 361-362 and Table 3).

### ***Conclusion***

7. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

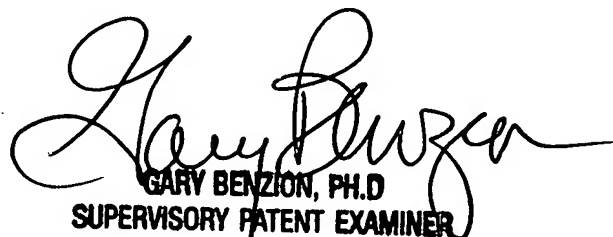
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

cbw



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